

REMARKS

The applicants have carefully studied the outstanding Office Action. The present response is intended to be fully responsive to all points of final rejection raised by the Examiner, and is believed to place the application in condition for allowance. Favorable reconsideration and allowance of the application are respectfully requested.

Claim rejections - 35 USC § 102

Claims 34 and 35 are rejected under 35 U.S.C. 102(a) as being anticipated by Kagalwala et al (Computational model of DIC microscopy for reconstructing 3-D specimens: from observations to measurement).

The applicants respectfully submit that the date of the Kagalwala et al reference is **May 25, 1999**, which is the date on which the paper was presented at the QELS '99 Conference. However, the present application is a National Phase filing of International PCT Application No. PCT/IL99/00645 filed on November 30, 1999, which claims priority from Israel Application No. 127,359 filed on December 1, 1998 and U.S. Application Serial No. 09/238,225 filed on January 27, 1999. The applicants therefore believe that both of these priority documents overcome the Kagalwala reference, and request withdrawal of the rejection of claims 34 and 35 under 35 U.S.C. 102(a).

Claims 40 and 41 are rejected under 35 U.S.C. 102(e) as being anticipated by Wolleschensky et al (US 6,771,417 B1). The Examiner states that:

"Wolleschensky teaches adaptive optics to correct for indices of refraction in a sample (column 1, lines 10-19 and 60-68, column 2, lines 7-15 and 30-33, column 3, line 58, column 4, lines 1-4, column 7, lines 55-62, column 8, lines 3-33 and lines 58-62."

The applicants respectfully submit that there is a fundamental difference between the invention described in Wolloschensky et al, and the claimed invention of the present application. In the Wolloschensky et al patent, to the best of the applicants'

understanding, there is described the use of a **two dimensional** adaptive optical element disposed only in the **illumination path**, while claims 40 and 41 of the present application recite the disposing **in the imaging path** of a **three dimensional medium** with refractive properties, that corrects aberrations arising from variations of the refractive index in the three dimensional sample.

While a two dimensional adaptive element can correct the aberrations at one point at a time and, depending on the sample, must be re-adjusted for each point separately, (as described by Wolleschensky et al. for focused laser illumination in a confocal-like microscope) the three dimensional medium recited in claims 40 and 41 can correct aberrations from a three dimensional sample for all of the imaged volume at once.

Furthermore, Wolleschensky et al. discusses the correction only of defocus aberrations (column 4, lines 30-38), which require fitting to high order spherical aberrations, and are not given in a closed form., and of aberrations caused by the substrate ("microtiter plate"). In the present application, methods and apparatus are described for determining the three-dimensional refractive index of the sample itself, directly from DIC or phase microscopy, and the use of the three-dimensional refractive indices to correct aberrations. In the claims of the parent application of this application, these three dimensional refractive indices are used to perform ray tracing, to obtain the three-dimensional point spread function used in the deconvolution process for determining the computational aberration correction. In addition to that use of the determined three-dimensional refractive indices, claims 40 and 41 of the present application, in contrast to what is shown in Wolleschensky, recite the utilization of these indices for insertion into a three-dimensional correcting medium, it being understood that the medium has inverse-refractive index characteristics, in order to correct the aberrated wavefront phases back to create an unaberrated wavefront.

In view of the above remarks, the applicants therefore respectfully submit that claims 40 and 41 are not anticipated by Wolleschensky et al., and respectfully request withdrawal of the 35 U.S.C. 102(e) rejection thereof.

Claim rejections - 35 USC § 103

Claims 40 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of White et al. (Aberration control in quantitative imaging of botanical specimens by multidimensional fluorescence microscopy) and Clark et al. (US 6,384,952 B1).

The Examiner has stated that:

"White discloses a method for confocal microscopy comprising the steps of: providing a confocal microscope ("confocal systems" at page 99, Summary) having an image information acquirer ("confocal measurements" at page 99, Summary; Confocal microscopy was carried out with out modified Bio-Rad MRC 600 system" at page 105, left column, bottom paragraph; the fact that confocal measurements are taken would have suggested to one skilled in the art that an image information acquirer was present) providing information relating to variations in the refractive index in a three-dimensional imaged volume ("Three-dimensional (x,y,z) volume images" and "section images" at page 105, right column, top paragraph; any image data depicted in a slice image is necessarily cause by and necessarily depicts variations of the indices of refraction within the specimen for each slice; e.g., refer to applicant's prior art figure 2), said microscope having an imaging path between a three-dimensional sample and said image information acquirer (inherent to a confocal microscope).

While White discloses correction for aberrations resulting from variations of the index of refraction of the three dimensional sample ("sample aberrations" at page 99, Summary; "estimation and correction of aberrations in confocal imaging" at page 99, Introduction, last sentence) by physically altering the measurement procedure ("spatial corrections ... interactively changing the parameters used for measurements along the z-axis" at page 109, left column, first sentence), White does not disclose:

disposing in said imaging path a three-dimensional medium with refractive properties that correcting the aberrations."

The examiner then brings the Clark reference which assertedly discloses: "a system of "adaptive optics" (column 1, line 19) for confocal microscopes ("confocal microscopes" at column 2, line 17), for correcting aberrations "aberration" at column 1, line 59; "correcting for these effects" at column 2, line 10), comprising disposing in the imaging path a three-dimensional medium with refractive properties that corrections for the aberrations ("a deformable mirror to apply the correction" at column 2, line 48)."

The Examiner then concludes that:

"It would have been obvious at the time the invention was made to one of ordinary skill in the art to provide the confocal microscope of White with the adaptive optics taught by Clark, in order to correct for White's aberrations to thereby enhance the optical performance of the microscope ("enhance the operational performance of the clinical microscopes in use today" at Clark, column 2, line 19) by correcting for wavefront distortion ("corrected wave" at White column 1, line 63)."

The applicants respectfully submit that the Examiner's interpretation of what is disclosed in Clark et al is erroneous.

The Clark patent describes a novel deformable mirror construction, which, is described as being suitable for adaptive optics applications for reducing the effects of aberrations, including in conventional and confocal microscopes. However, a distortable mirror is essentially operative as a two dimensional device, defined by the surface of the mirror, and even if it were to be asserted that the surface deformation, regardless of how small it is in comparison with the lateral dimensions of the mirror, essentially make it a three dimensional device, it can certainly not be described as having refractive properties. Therefore, nowhere in Clark, to the best of the applicants' understanding, is there mentioned or suggested "a three-dimensional medium with refractive properties that correct aberrations" as recited in claims 40 and 41 of the present application.

Furthermore, the applicants respectfully disagree with the conclusion drawn by the Examiner that "it would have been obvious at the time the invention was made to one of ordinary skill in the art to provide the confocal microscope of White with the adaptive optics taught by Clark, in order to correct for White's aberrations to thereby enhance the optical performance of the microscope ...". The applicants submit that the generic form of "adaptive optics taught by Clark", i.e. deformable mirrors, (as opposed to the specific patented mirrors of Clark et al) had been known in the art for many years before **both** Clark and White. Consequently, if as implied by the Examiner, it were obvious to incorporate such adaptive optics into the confocal microscope of

White, to arrive at the subject matter of claims 40 and 41 of the present invention, it is not clear why White himself did not suggest doing so.

In view of the above remarks, the applicants therefore respectfully submit that claims 40 and 41 are not rendered obvious by combination of White et al. with Clark et al., and respectfully request withdrawal of the 35 U.S.C. 103(a) rejection thereof.

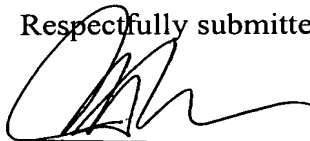
Claims 38 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Clark et al. (US 6,384,952 B1) and Kagalwala et al (Computational model of DIC microscopy for reconstructing 3-D specimens: from observations to measurement).

As previously mentioned, the applicants believe that the priority applications claimed by the present application, overcome the Kagalwala reference, which cannot therefore be properly used in this 35 U.S.C. 103(a) rejection, and withdrawal thereof is respectfully requested.

Conclusion

For all of the reasons set forth above, applicants respectfully submit that all of the pending claims 34, 35 and 38-41 are believed to be allowable. Reconsideration and prompt allowance of this application are therefore respectfully requested.

Respectfully submitted,



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